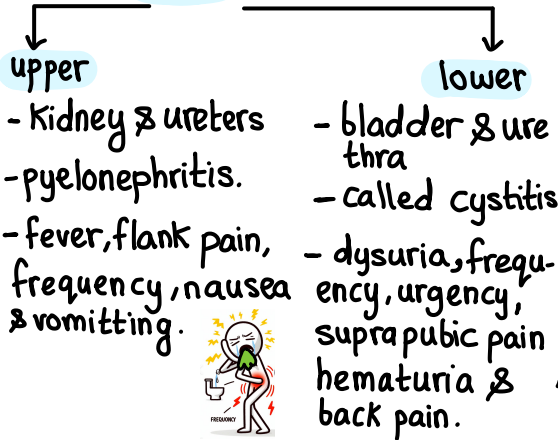


# pharmacology of the UTi

## ① UTis:

- ① ↑ affects females in child-bearing age.
- ② 60% of females will get infected in their lifetime & 1/4 will have recurrence within a year.

## ③ utis



④ complicated	un-complicated
occurs in patients who have predisposing lesions of the urinary tract (stones, congenital abnormalities, catheters, obstructions.....).	occurs in patients who have a healthy urinary tract.

\* E.coli is the most common bacteria involved, however any type of other bacteria can cause it too.

## ② Antibiotics for UTis:

- cephalosporins
- Nitrofurantoin
- fosfomycin
- Trimthoprim-sulphamethoxazole (co-trimoxazole).
- Quinolones & Fluoroquinolones

\* Cats need fun Queens for tea parties.



## Quinolones & fluoroquinolones

### ① mechanism of action

inhibit microbial DNA synthesis by inhibiting bacterial gyrase enzyme which is a type 2 topoisomerase.

- ② their use has been reduced due to:
  - ① toxicity.
  - ② development of resistance.
  - ③ new safer microbials.

### ③ features:





- ① they're chemotherapeutic agents
- ③ broad spectrum → pseudomonas.
- ② cidal

### ④ side effects.

- GIT irritation; photosensitivity	- Some have been reported to be carcinogens
- Some are not recommended in children or during pregnancy because they may interfere with cartilage development	- Cardiac toxicity (many may be associated with prolongation of QT interval) (many were withdrawn because of this side effect)

## 5 Classifications.

★ most used ones

<h3>1st generation</h3> <p>① Nalidixic acid:</p> <ul style="list-style-type: none"><li>- ↑ effective in G-ve infections.</li><li>- only in UTIs.</li><li>- good activity against: E. coli, proteus, shigella, Enterobacter &amp; Klebsiella </li><li>- No effect against pseudomonas.</li><li>- little effect against G+ve bacteria.</li></ul> <p>② piperidic acid. </p> <p>③ oxolinic acid.</p>	<h3>2nd generation</h3> <p>① Ciprofloxacin ★ ② Ofloxacin</p> <p>③ Norfloxacin ④ Enoxacin.</p> <p>⑤ Lomefloxacin. ⑥ Nadifloxacin.</p> <p><i>*all exhibit more activity against G+ve &amp; G-ve bact.</i></p>  <p>*lemon cone</p>
<h3>3rd generation</h3> <p>① Levofloxacin ★</p> <p>② Sparfloxacin</p> <p>③ Gatifloxacin</p>	<h3>4th generation.</h3> <p>① Moxifloxacin. ★</p> <p>② Prulifloxacin.</p> <p>③ Gemifloxacin. </p>
3, 4 generations have good activity against pseudomonas & anaerobic micro-organisms	

**Note:** Ciprofloxacin & levofloxacin are mainly used in complicated UTIs, respiratory infections, invasive external otitis, bacterial prostatitis, cervicitis & bacterial diarrhoea caused by shigella, salmonella & E. coli.

● **Note:** quinolones are orally effective & well absorbed but affected by food containing  $Ca^{2+}$  & iron.

## ⑥ mechanisms of bacterial resistance to quinolones

some types of bacterial efflux pumps  
↓ intracellular quinolones concentration.

produce proteins that can bind to DNA gyrase by G-ve bact. protecting it from quinolones.

mutations in DNA gyrase/topoisomerase → ↓ in quinolone binding affinity → ↓ its effectiveness.

# Nitrofurantoin

\*Synthetic bactericidal orally effective antibiotic.

## ① Effectiveness:

① against G+ve & G-ve Bacteria.

② E-coli.

③ In Utis (cystitis), known as "Ut antiseptic" in this case.

## ② Moa:

It is converted by bacterial reductases into many reactive intermediates leading to direct damaging effect of bacterial DNA, disruption of RNA and protein synthesis and also interfering with many metabolic processes in bacteria

## ③ features:

- Development of resistance to nitrofurantoin is rare, due to multiple sites of action (the bacteria that is sensitive to it remain sensitive forever)
- Pulmonary fibrosis is a major side effect to nitrofurantoin
- Nitrofurantoin is contraindicated in patients with G-6-PD deficiency

# Fosfomycin

It is a broad-spectrum bactericidal drug primarily used to treat lower UTI (cystitis) and occasionally is used for prostate infections

It disrupts cell wall synthesis by inhibiting phosphoenolpyruvate synthetase and thus interferes with the production of peptidoglycan

Fosfomycin has a broad spectrum of activity against both gram-positive and gram-negative organisms, including many antibiotic-resistant organisms

It is available in 3g oral powder dosage form for reconstitution

Use of fosfomycin is commonly restricted to only a single dose because of rapid microbial resistance

## Side effects:

- Metallic taste
- Stomach upset
- Dizziness
- Stuffy nose
- Back pain
- Vaginal itching or discharge

